Application No. 09/620,038
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Clean Version of Replacement Claims for Entry During Prosecution of US Application No. 09/620,038

23. A method for continuously determining a glucose concentration in a body fluid with glucose-containing perfusate, the method comprising the steps of:

providing a microdialysis probe, a measurement cell, and a control device,

inserting the microdialysis probe into the body fluid,

passing the perfusate having a starting content of glucose through the microdialysis probe to obtain a dialysate,

transporting the dialysate to the measuring cell,

obtaining measurement signals that correlate with a glucose content of the dialysate in the measuring cell,

measuring the measurement signals that correlate with the glucose content of the dialysate,

adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, and

determining the glucose concentration in the body fluid by either using a momentary starting content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals.

24. The method of claim 23 wherein a value of the base line signal is a controlled variable and the adjusting step includes determining a momentary starting content of the glucose in the perfusate as a measure for the glucose content of the body fluid when a deviation of a controlled variable from the command variable is negligible.

25. The method of claim 24 wherein the control device includes an adjuster having an adjusting variable and the adjusting step includes initially determining the starting content of glucose in the perfusate by comparing the adjusting variable with corresponding normalized values of the glucose concentration in the body fluid.

26. The method of claim 23 wherein the control device includes an adjuster having an adjusting variable and the adjusting step includes initially determining the

starting content of glucose in the perfusate by comparing the adjusting variable with corresponding normalized values of the glucose concentration in the body fluid.

27. The method of claim 23 further comprising the step of measuring the glucose content of the perfusate before it is passed into the microdialysis probe.

28. The method of claim 24 further comprising the step of measuring the glucose content of the perfusate before it is passed into the microdialysis probe.

29. The method of claim 26 further comprising the step of measuring the glucose content of the perfusate before it is passed into the microdialysis probe.

30. The method of claim 23 further comprising the step of flow mixing two perfusion liquids with different glucose concentrations provided in two separate reservoirs to influence the starting content of glucose in the perfusate.

31. The method of claim 24 further comprising the step of flow mixing two perfusion liquids with different glucose concentrations provided in two separate reservoirs to influence the starting content of glucose in the perfusate.

32. The method of claim 27 further comprising the step of flow mixing two perfusion liquids with different glucose concentrations provided in two separate reservoirs to influence the starting content of glucose in the perfusate.

33. The method of claim 23 wherein the perfusate is passed through the microdialysis probe in alternating successive transport and dialysis intervals at different flow rates, the flow rate during the transport intervals being higher than during the dialysis intervals.

34. The method of claim 24 wherein the perfusate is passed through the microdialysis probe in alternating successive transport and dialysis intervals at different flow rates, the flow rate during the transport intervals being higher than during the dialysis intervals.

35. The method of claim 27 wherein the perfusate is passed through the microdialysis probe in alternating successive transport and dialysis intervals at different flow rates, the flow rate during the transport intervals being higher than during the dialysis intervals.

36. The method of claim 30 wherein the perfusate is passed through the microdialysis probe in alternating successive transport and dialysis intervals at different

flow rates, the flow rate during the transport intervals being higher than during the dialysis intervals.

37. The method of claim 33 wherein the flow rate during the transport intervals is increased to such an extent that the starting content of glucose in the perfusate during passage through the microdialysis probe remains essentially constant and that during the dialysis intervals the transport is interrupted or at least the flow rate is reduced to such an extent that the glucose concentration of the dialysate approximates the glucose content of the body fluid.

38. The method of claim 23 wherein the command variable is determined by integration or differentiation of the time course of the measurement signals.

39. The method of claim 24 wherein the command variable is determined by integration or differentiation of the time course of the measurement signals.

40. The method of claim 27 wherein the command variable is determined by integration or differentiation of the time course of the measurement signals.

41. The method of claim 30 wherein the command variable is determined by integration or differentiation of the time course of the measurement signals.

42. The method of claim 33 wherein the command variable is determined by integration or differentiation of the time course of the measurement signals.

43. The method of claim 38 wherein the command variable is determined by qualitative detection of signal peaks in the time course of the measurement signals.

44. The method of claim 33 wherein the command variable is determined by comparing the actual signal curve of the measurement signals with calibrated signal patterns deposited in a storage medium.

45. The method of claim 38 wherein the command variable is determined by comparing the actual signal curve of the measurement signals with calibrated signal patterns deposited in a storage medium.

46. The method of claim 33 wherein the command variable is determined from the peak value of the signal time course of the measurement signals during each transport interval.

47. The method of claim 38 wherein the command variable is determined from the peak value of the signal time course of the measurement signals during each transport interval.

48. The method of claim 33 wherein the command variable is determined according to the glucose content c of the body fluid according to the relationship

$$c = \left[\frac{S_g}{S_g \cdot (1 - b) + b \cdot S_0} - 1 \right] \cdot a \cdot c_0 + c_0$$

in which S_g denotes a peak value of the measurement signal and S_0 denotes a base line value of the signals measured during a transport interval of the perfusate passing through the microdialysis probe and c_0 is the momentary starting content of glucose in the perfusate and a, b are empirically determined correction factors compensating for diffusion and mixing and remaining recovery effects during the transport interval.

49. The method of claim 38 wherein the command variable is determined according to the glucose content c of the body fluid according to the relationship

$$c = \left[\frac{S_g}{S_g \cdot (1 - b) + b \cdot S_0} - 1 \right] \cdot a \cdot c_0 + c_0$$

in which S_g denotes a peak value of the measurement signal and S_0 denotes a base line value of the signals measured during a transport interval of the perfusate passing through the microdialysis probe and c_0 is the momentary starting content of glucose in the perfusate and a, b are empirically determined correction factors compensating for diffusion and mixing and remaining recovery effects during the transport interval.

50. The method of claim 23 further comprising a step of regulating discontinuously the starting content of glucose in the perfusate by a two-point control process in which the starting content of glucose in the perfusate is changed by a predetermined adjustment value when there is a control deviation.

68. A method for continuously determining a glucose concentration in a body fluid with glucose-containing perfusate, the method comprising the steps of:

providing a microdialysis probe, a measurement cell, and a control device,

inserting the microdialysis probe into the body fluid,

passing the perfusate having a starting content of glucose through the microdialysis probe at different flow rates to obtain a dialysate,

transporting the dialysate to the measuring cell,

obtaining measurement signals that correlate with the glucose content of the dialysate in the measuring cell,

measuring the measurement signals that correlate with the glucose content of the dialysate,

adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, and

determining the glucose concentration in the body fluid by either using a momentary starting content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals.

69. The method of claim 68 wherein a value of the base line signal is a controlled variable and the adjusting step includes determining a momentary starting content of the glucose in the perfusate as a measure for the glucose content of the body fluid when a deviation of a controlled variable from the command variable is negligible.

70. The method of claim 69 wherein the control unit includes an adjuster having an adjusting variable and the adjusting step includes initially determining the starting content of glucose in the perfusate by comparing the adjusting variable with corresponding normalized values of the glucose concentration in the body fluid.

71. The method of claim 68 further comprising the step of measuring the glucose content of the perfusate before the perfusate is passed into the microdialysis probe.

72. The method of claim 68 further comprising the step of flow mixing two perfusion liquids with different glucose concentrations provided in two separate reservoirs to influence the starting content of glucose in the perfusate.

73. The method of claim 68 wherein the perfusate flows through the microdialysis probe during transport intervals and dialysis intervals, the flow rate during

the transport intervals is greater than the flow rate during the dialysis intervals and is such that the starting content of glucose in the perfusate during passage through the microdialysis probe remains essentially constant and that during the dialysis intervals the transport of the perfusate is interrupted or at least the flow rate is reduced to such an extent that the glucose concentration of the dialysate approximates the glucose content of the body fluid.

74. The method of claim 73 wherein the command variable is determined from a peak value of a signal time course of the measurement signals during each transport interval.

75. The method of claim 68 wherein the command variable is determined from a peak value of a signal time course of the measurement signals.

76. The method of claim 68 wherein the command variable is determined according to the glucose content c of the body fluid according to the relationship

$$c = \left[\frac{S_g}{S_g \cdot (1-b) + b \cdot S_0} - 1 \right] \cdot a \cdot c_0 + c_0$$

in which S_g denotes a peak value of the measurement signal and S_0 denotes a base line value of the signals measured during a transport interval of the perfusate passing through the microdialysis probe and c_0 is the momentary starting content of glucose in the perfusate and a, b are empirically determined correction factors compensating for diffusion and mixing and remaining recovery effects during the transport interval.

77. (The method of claim 68 wherein the command variable is determined by integration or differentiation of a time course of the measurement signals.

78. The method of claim 68 wherein the command variable is determined by comparing an actual signal curve of the measurement signals with calibrated signal patterns deposited in a storage medium.

79. The method of claim 68 further comprising a step of regulating discontinuously the starting content of glucose in the perfusate by a two-point control process in which the starting content of glucose in the perfusate is changed by a predetermined adjustment value when there is a control deviation.